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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,494	12/13/2000	Nikolich Zugich	MSK.P-042	2225

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,494	ZUGICH ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/13.00, 11/4/02 & 2/27/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *5,6,10,15 and 17-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-9,11-13 and 16* is/are rejected.

7)☒ Claim(s) *14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3 & 9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Rec'd 3/29/04 & 7/19/04

DETAILED ACTION

1. Applicant's amendments filed 12/13/00, 11/4/02 and 2/27/03 are acknowledged and have been entered.

Claims 1-33 are pending.

2. Applicant's election with traverse of Group I (claims 1-4, 7-9 and 11-16), and species of SEQ ID NO: 12 from gp75 in Applicant's amendment filed 2/27/03 is acknowledged.

The basis for the traversal of lack of unity is that Bakker et al do not teach that the gp100 peptide is weakly immunogenic, and that the gp100 peptide taught by Bakker et al is not weakly immunogenic within the meaning of the application. Applicant points to page 3 of the instant specification at lines 19-20.

Applicant's arguments have been fully considered but are not persuasive. It is the Examiner's position that the disclosure at lines 19 and 20 on page 3 of the instant specification states "inherently non-immunogenic or only weakly immunogenic in the host, and are unable to induce activation and differentiation of effector CTLS." The disclosure continues "Such antigens therefore are of at most limited therapeutic utility in conventional approaches to immunotherapy." It is the Examiner's position that "weakly immunogenic" means that an immune response is generated. No term maybe given a meaning repugnant to the usual meaning of the term (MPEP 608.01(o)). It is the Examiner's further position that Bakker et al teach the gp100 wild-type peptide required 10 fold higher concentration to be recognized by a TIL cell line. In addition, the prior art reference Lipford et al, WO 95/29193 and Huard et al (below) all teach the method of instant claim 1.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claim 15 (non-elected species of Group I) and claims 5, 6, 10 and 17-33 (non-elected groups II-IX) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-4, 7-9 and 11-14 read on the elected species, SEQ ID NO: 12.

Upon consideration of a search, since SEQ ID NO: 12 appears to be free of the prior art, the search has been extended to include SEQ ID NO: 10 recited in claim 16.

Claims 1-4, 7-9, 11-14 and 16 are currently being examined.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 7 and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is a substantial duplicates of claim 3, and Claim 8 is a substantial duplicate of claim 4. There appears to be no difference in scope.

5. For the purpose of prior art rejections, the filing date of the instant claims 2, 4 and 8 is deemed to be the filing date of PCT/US99/13146, i.e. 6/11/99, as the parent applications do not support the claimed limitations of the instant application. The limitation "each consist of from 8 to 14 amino acids " is only disclosed in PCT application.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 9, 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/29193, IDS reference) as evidenced by Overwijk et al (J. Exp. Med. 188(2) 277-286, 1998, IDS reference).

WO 95/29193 teaches a method of inducing an immune response by administering heteroclitic peptides from tumor antigens, including gp100, altered to improve peptide MHC class I (including HLA-A2.1) binding affinity and to render the peptide capable of inducing an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell") whereas it had not been immunogenic prior to alteration (especially introduction and last paragraph on page 302). The peptides are 8 amino acid residues in length, i.e., "from 8 to 14 amino acids". WO 95/29193 teaches that some of the wild-type peptides induce a partial response or no response at all as measured by recognition by HLA-A2 restricted TIL, i.e., are "weakly immunogenic" (especially

Tables, Table 11). The peptides taught by WO 95/29193 are "from 8 to 14 amino acids" in length.

Overwijk et al teach many tumor-associated antigens are poorly immunogenic tissue differentiation antigens, i.e., they are weakly immunogenic. Overwijk et al teaches gp100 is expressed by normal melanocytes and the majority of malignant melanomas and that CTL with reactivity to gp100 have been detected in patients with metastatic melanoma (especially column 1 on page 278). Claim 12 is included in this rejection because it is an inherent property of gp100 that it is expressed in normal and tumor tissues.

8. Claims 1, 2, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lipford et al (Immunology 84(2), 1995, 298-303, IDS reference).

Lipford et al teach a method of inducing an immune response by administering a heteroclitic peptide YIFAFRDL which was altered from HPV E6 peptide YDFAFRDL at position 2 to improve peptide MHC class I H-2Kb binding affinity, and to render it capable of inducing an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell") whereas it had not been immunogenic prior to alteration (especially introduction and last paragraph on page 302). The peptides are 8 amino acid residues in length, i.e., "from 8 to 14 amino acids".

9. Claim 2 is rejected under 35 U.S.C. 102(a) as being anticipated by Dyall et al (J. Exp. Med 188(9), 1553-1561, 11/2/98, IDS reference).

Dyall et al teach a method for inducing a cellular immune response to a heteroclitic peptide SSIEFARL (i.e., the therapeutic antigen) (hsV-8), which is a variant of peptide SEIEFARL (i.e., the target antigen) which binds poorly to the murine class I MHC molecule H-2Kb and which due to poor binding cannot elicit a CTL response in Kb-bearing B6 mice (especially paragraph spanning columns 1 and 2 on page 1555) and also to a heteroclitic variant TAYRYHLL of peptide TWHRYHLL from gp75 which displayed poor binding similar to the SEIEFARL peptide (especially page 1557). Both heteroclitic peptides bound with greater affinity than the target peptides to Kb and they are both 8 amino acid residues in length, i.e., "from 8 to 14 amino acids", and the heteroclitic peptides were designed to bind to MHC with greater affinity than the target peptides without alteration of the immune recognition portion (especially column 1 on page 1554).

10. Claims 1, 2, 9 and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Huard et al (Int. Immunol. 9(11), 1997, 1701-1701) as evidenced by admissions in the instant specification on page 13 at lines 20-23.

Huard et al teach a method for inducing a cellular immune response in Kbm8-bearing mice to a heteroclitic peptide SEIEFARL (i.e., the therapeutic antigen) (hsV-8), which is a variant of peptide SSIEFARL (i.e., the target peptide). The target peptide

SSIEFARL cannot elicit a CTL response in Kbm8-bearing mice (especially Table 1 on page 1705). The heteroclitic peptide bound with greater affinity than the target peptide to Kbm8 and it is 8 amino acid residues in length, i.e., "from 8 to 14 amino acids", and the heteroclitic peptide was designed to bind to MHC with greater affinity than the target peptide without alteration of the immune recognition portion and it induced an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell"). Huard et al further teach that SSIEFARL (i.e., the therapeutic antigen) binds to MHC class I molecule Kb in Kb-bearing B6 mice and further teaches a method for inducing an immune response using the said peptide in Kb-bearing mice. Huard et al teach that the said peptide does not induce an immune response in Kbm8 bearing mice, whereas SEIEFARL (i.e., the target peptide) does.

The admissions in the specification on page 13 at lines 20-23 is that the SSI (i.e., SSIEFARL) peptide is a heteroclitic vaccine peptide and that SEI (i.e., SEIEFARL) is the parental peptide [or "target" peptide] in B6 mice.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 2, 4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dyall et al (J. Exp. Med 188(9), 1553-1561, 11/2/98, IDS reference) in view of Anderson et al (J. Exp. Med. 174, 8/1991, 489-492, IDS reference) and Yewdell et al (J. Immunol. 152, 1994, 1163-1170, IDS reference).

Dyall et al teach a method for inducing a cellular immune response to a heteroclitic peptide SSIEFARL (i.e., the therapeutic antigen) (hsV-8), which is a variant of peptide SEIEFARL (i.e., the target antigen) which binds poorly to the murine class I MHC molecule H-2Kb and which due to poor binding cannot elicit a CTL response in Kb-bearing B6 mice (especially paragraph spanning columns 1 and 2 on page 1555) and

also to a heteroclitic variant TAYRYHLL of peptide TWHRYHLL from gp75 which displayed poor binding similar to the SEIEFARL peptide (especially page 1557). Both heteroclitic peptides bound with greater affinity than the target peptides to Kb and they are both 8 amino acid residues in length, i.e., "from 8 to 14 amino acids", and the heteroclitic peptides were designed to bind to MHC with greater affinity than the target peptides without alteration of the immune recognition portion (especially column 1 on page 1554). Dyall et al teach fusion proteins encoded by ERIS (i.e., ER sorting/ trafficking signal)-containing minigenes have been shown to insert the attached class I binding peptides into the ER for presentation by Class I MHC (especially column 1 on page 1556).

Dyall et al do not teach the claimed method wherein the therapeutic antigen further comprises an ER trafficking signal.

Anderson et al teach a peptide preceeded by an endoplasmic reticulum translocation signal (i.e., ER sorting/trafficking signal) and the importance of peptide transport into the ER for expression of class I MHC-peptide complexes for induction of immune response.

Yewdell et al teach antigenic peptides carboxy terminal to an ER insertion sequence and the importance of the ER insertion sequence in delivering the peptide to the ER for peptide/MHC class I expression at the cell surface.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a heteroclitic peptide connected to an ER sorting/trafficking signal as taught by Anderson et al or Yewdell et al or Dyall et al to be used in the method of Dyall et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to more efficiently induce an immune response to the heteroclitic peptide in the method of Dyall et al given the teachings of Anderson et al and Yewdell et al of the importance of peptide transport into the ER for expression of class I MHC-peptide complexes at the cell surface.

13. Claims 1-4, 7-9, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/29193 (IDS reference) in view of Anderson et al (J. Exp. Med. 174, 8/1991, 489-492, IDS reference) and Yewdell et al (J. Immunol. 152, 1994, 1163-1170, IDS reference).

WO 95/29193 teaches a method of inducing an immune response by administering heteroclitic peptides from tumor antigens, including gp100, altered to improve peptide MHC class I (including HLA-A2.1) binding affinity and to render the peptide capable of inducing an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell") whereas it had not been immunogenic prior to alteration (especially introduction and last paragraph on page 302). The peptides are 8 amino acid residues

in length, i.e., "from 8 to 14 amino acids". WO 95/29193 teaches that some of the wild-type peptides induce a partial response or no response at all as measured by recognition by HLA-A2 restricted TIL, i.e., are "weakly immunogenic" (especially Tables, Table 11). The peptides taught by WO 95/29193 are "from 8 to 14 amino acids" in length.

WO 95/29193 does not teach the claimed method wherein the therapeutic antigen further comprises an ER trafficking signal.

Anderson et al teach a peptide preceeded by an endoplasmic reticulum translocation signal (i.e., ER sorting/trafficking signal) and the importance of peptide transport into the ER for expression of class I MHC-peptide complexes for induction of immune response.

Yewdell et al teach antigenic peptides carboxy terminal to an ER insertion sequence and the importance of the ER insertion sequence in delivering the peptide to the ER for peptide/MHC class I expression at the cell surface.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a heteroclitic peptide connected to an ER sorting/trafficking signal as taught by Anderson et al or Yewdell et al to be used in the method of WO 95/29193.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to more efficiently induce an immune response to the heteroclitic peptide in the method of WO 95/29193 given the teachings of Anderson et al and Yewdell et al of the importance of peptide transport into the ER for expression of class I MHC-peptide complexes at the cell surface. Claim 12 is included in this rejection because gp100 is expressed in normal and tumor tissues.

14. Claims 1-4, 7-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipford et al Immunology 84(2), 1995, 298-303, IDS reference).
in view of Anderson et al (J. Exp. Med. 174, 8/1991, 489-492, IDS reference) and Yewdell et al (J. Immunol. 152, 1994, 1163-1170, IDS reference).

Lipford et al teach a method of inducing an immune response by administering a heteroclitic peptide YIFAFRDL which was altered from HPV E6 peptide YDFAFRDL at position 2 to improve peptide MHC class I H-2Kb binding affinity, and to render it capable of inducing an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell") whereas it had not been immunogenic prior to alteration (especially introduction and last paragraph on page 302). The peptides are 8 amino acid residues in length, i.e., "from 8 to 14 amino acids".

Lipford et al do not teach the claimed method wherein the therapeutic antigen further comprises an ER trafficking signal.

Anderson et al teach a peptide preceeded by an endoplasmic reticulum translocation signal (i.e., ER sorting/trafficking signal) and the importance of peptide transport into the ER for expression of class I MHC-peptide complexes for induction of immune response.

Yewdell et al teach antigenic peptides carboxy terminal to an ER insertion sequence and the importance of the ER insertion sequence in delivering the peptide to the ER for peptide/MHC class I expression at the cell surface.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a heteroclitic peptide connected to an ER sorting/trafficking signal as taught by Anderson et al or Yewdell et al to be used in the method of Lipford et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to more efficiently induce an immune response to the heteroclitic peptide in the method of Lipford et al given the teachings of Anderson et al and Yewdell et al of the importance of peptide transport into the ER for expression of class I MHC-peptide complexes at the cell surface.

15. Claims 1, 2, 9 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huard et al (Int. Immunol. 9(11), 1997, 1701-1701) in view of admissions in the specification on page 13 at lines 20-23.

Huard et al teach a method for inducing a cellular immune response to a heteroclitic peptide SEIEFARL (i.e., the therapeutic antigen) (hsV-8), which is a variant of peptide SSIEFARL (i.e., the target antigen) cannot elicit a CTL response in Kbm8-bearing mice (especially Table 1 on page 1705). The heteroclitic peptide bound with greater affinity than the target peptide to Kbm8 and it is 8 amino acid residues in length, i.e., "from 8 to 14 amino acids", and the heteroclitic peptide was designed to bind to MHC with greater affinity than the target peptide without alteration of the immune recognition portion and it induced an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell"). Huard et al further teach that SSIEFARL binds to MHC class I molecule Kb in Kb-bearing mice and induces an immune response. It does not bind to induce an immune response in Kbm8 bearing mice, whereas SEIEFARL does.

Huard et al do not teach a method wherein the method for inducing a cellular immune response comprises administration of a therapeutic antigen that is SSIEFARL (SEQ ID NO: 10 of the instant application).

The admissions in the specification on page 13 at lines 20-23 is that the SSI (i.e., SSIEFARL) peptide is a heteroclitic vaccine peptide and that SEI (i.e., SEIEFARL) is the parental peptide in B6 mice.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have induced an immune response similar to the response taught by Huard et al in Kbm8-bearing mice by altering the method of Huard et al to use Kb-bearing mice and to have substituted the peptide SSIEFARL for SEIEFARL, i.e., to have used the peptide SSIEFARL as the therapeutic antigen.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to induce an immune response to HSV in Kb-bearing mice.

16. Claims 1-4, 7-9 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huard et al (Int. Immunol. 9(11), 1997, 1701-1701) in view of admissions in the specification on page 13 at lines 20-23 and further in view of Anderson et al (J. Exp. Med. 174, 8/1991, 489-492, IDS reference) and Yewdell et al (J. Immunol. 152, 1994, 1163-1170, IDS reference).

Huard et al teach a method for inducing a cellular immune response in Kbm8-bearing mice to a heteroclitic peptide SEIEFARL (i.e., the therapeutic antigen) (hsV-8), which is a variant of peptide SSIEFARL (i.e., the target peptide). The target peptide SSIEFARL cannot elicit a CTL response in Kbm8-bearing mice (especially Table 1 on page 1705). The heteroclitic peptide bound with greater affinity than the target peptide to Kbm8 and it is 8 amino acid residues in length, i.e., "from 8 to 14 amino acids", and the heteroclitic peptide was designed to bind to MHC with greater affinity than the target peptide without alteration of the immune recognition portion and it induced an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell"). Huard et al further teach that SSIEFARL (i.e., the therapeutic antigen) binds to MHC class I molecule Kb in Kb-bearing B6 mice and further teaches a method for inducing an immune response using the said peptide in Kb-bearing mice. Huard et al teach that the said peptide does not induce an immune response in Kbm8 bearing mice, whereas SEIEFARL (i.e., the target peptide) does.

The Huard not teach the claimed method wherein the therapeutic antigen further comprises an ER trafficking signal and Huard et al do not teach that the SEIEFARL peptide is the parental peptide in B6 mice.

The admissions in the specification on page 13 at lines 20-23 is that the SSI (i.e., SSIEFARL) peptide is a heteroclitic vaccine peptide and that SEI (i.e., SEIEFARL) is the parental peptide [or "target" peptide] in B6 mice.

Anderson et al teach a peptide preceeded by an endoplasmic reticulum translocation signal (i.e., ER sorting/trafficking signal) and the importance of peptide transport into the ER for expression of class I MHC-peptide complexes for induction of immune response.

Yewdell et al teach antigenic peptides carboxy terminal to an ER insertion sequence and the importance of the ER insertion sequence in delivering the peptide to the ER for peptide/MHC class I expression at the cell surface.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a heteroclitic peptide connected to an ER sorting/trafficking signal as taught by Anderson et al or Yewdell et al to be used in the method of the combination of Huard et al given the above-cited admissions in the instant specification.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to more efficiently induce an immune response to the heteroclitic peptide in the method of the combination of Huard et al given the teachings of Anderson et al and Yewdell et al of the importance of peptide transport into the ER for expression of class I MHC-peptide complexes at the cell surface.

17. Claims 1, 2, 9 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/29193, IDS reference) in view of U.S. Patent No. 6,328,969 B1.

WO 95/29193 teaches a method of inducing an immune response by administering heteroclitic peptides from tumor antigens, including gp100, altered to improve peptide MHC class I, including HLA-A2.1, binding affinity and to render it capable of inducing an immune response (i.e., "immune recognition domain binds to a cytotoxic T cell") whereas it had not been immunogenic prior to alteration (especially introduction and last paragraph on page 302). The peptides are 8 amino acid residues in length, i.e., "from 8 to 14 amino acids". WO 95/29193 teaches that some of the wild-type peptides induce a partial response or no response at all as measured by recognition by HLA-A2 restricted TIL, i.e., are "weakly immunogenic" (especially Tables, Table 11). The peptides taught by WO 95/29193 are "from 8 to 14 amino acids" in length.

WO 95/29193 does not teach a method comprising administration of heteroclitic peptides from gp75.

U.S. Patent No. 6,328,969 B1 discloses many tumor-associated antigens that are differentiation antigens shared by normal and tumor tissues are poorly immunogenic or not at all, i.e., they have weak immunogenicity or are non-immunogenic. U.S. Patent No. 6,328,969 B1 further discloses that gp75 is one such differentiation antigen, as well as CD20 (especially background of the invention) and further teaches the desirability of altering the peptide or protein to use it as a therapeutic antigen to elicit a strong immune response (especially column 4 at lines 37-40).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a peptide from a weakly or non-immunogenic differentiation antigen such as gp75 disclosed U.S. Patent No. 6,328,969 B1 in the

method taught by WO 95/29193 for inducing an immune response to a weak or non-immunogenic peptide from a tumor antigen.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because U.S. Patent No. 6,328,969 B1 discloses that gp75 is one of a class of weakly or non-immunogenic differentiation antigens and that it is desirable to alter the gp75 in order to induce an immune response and because WO 95/29193 Teaches a method of inducing an immune response to another weakly immunogenic tumor antigen by way of altering the target antigenic peptide.

18. Claim 14 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

19. The reference WO 95/29193 in Applicant's IDS filed 3/28/01 was crossed out by the Examiner because it is a duplicate listing of the same reference in Applicant's IDS filed 7/19/02.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is 703-308-0061. The examiner can normally be reached on Monday, Wednesday and Friday afternoons.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
June 2, 2003

CHRISTINA CHAN
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TECHNOLOGY CENTER 1600